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MDSP-P01-001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Moran et al.

Serial No.: 09/897,787

Group Art Unit: 1645

Filed: June 29, 2001

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Title: GRF2 BINDING PROTEINS AND APPLICATIONS THEREOF

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INFORMATION DISCLOSURE STATEMENT UNDER 37C.F.R 1.97(b)

Submitted herewith on Form PTO-1449 is a list of documents known to Applicants, their Agent and/or Attorney in compliance with the requirements of 37 C.F.R. 1.56. A copy of each document listed is also being submitted herewith.

This Information Disclosure Statement is being filed before the mailing of the first office action on the merits; therefore, no fee is due.

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Applicants respectfully request that the Examiner consider the listed documents and indicate that they were considered by making appropriate notations on the attached Form PTO-1449.

This submission does not represent that a search has been made or that no better art exists. Nor does it constitute an admission that each or all of the listed documents are material or constitute "prior art." If the Examiner applies any of the documents as prior art against any claim in the application and applicants determine that the cited documents do not constitute "prior art" under United States law, Applicants reserve the right to present to the Office the relevant facts and law regarding the appropriate status of such documents.

Applicants further reserve the right to take appropriate action to establish the patentability of the disclosed invention over the listed documents, should one or more of the documents be applied against the claims of the present application.

If there are any fees due in connection with the filing of this Statement, please charge the fees to our **Deposit Account, No. 18-1945.**

Respectfully submitted,
Ropes & Gray

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	Applicant Moran et al.	
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U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE

FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	Translation YES	Translation NO

OTHER DOCUMENTS
(Including Author, Title, Date, Pertinent Pages Etc.)

	AA	Aebersold, 1993, "Mass spectrometry of proteins and peptides in biotechnology", Curr. Opin. Biotechnol. **4**:412-419
	AB	Anborgh et al., 1999, "Ras-specific exchange factor GRF: oligomerization through its Dbl homology domain and calcium-dependent activation of Raf", Mol. Cell. Biol. **19**:4611-4622
	AC	Arnott et al., 1993, "Mass spectrometry of proteins and peptides: sensitive and accurate mass measurement and sequence analysis", Clin. Chem. **39**:2005-2010
	AD	Bos, 1998, "All in the family? New insights and questions regarding interconnectivity of Ras, Rap1 and Ral", Embo J. **17**:6776-6782
	AE	Buday and Downward, 1993, "Epidermal growth factor regulates $p21^{Ras}$ through the formation of a complex of receptor, Grb2 adaptor protein, and SOS nucleotide exchange factor", Cell **73**:611-620
	AF	Cen et al., 1992, "Isolation of multiple mouse cDNAs with coding homology to Saccharomyces cerevisiae CDC25: identification of a region related to Bcr, Vav, Dbl and CDC24", EMBO J. **11**:4007-4015
	AG	Cerione and Zheng, 1996, "The Dbl family of oncogenes", Curr. Op. Cell Biol. **8**:216-222
	AH	Chardin et al., 1993, "Human sos1 - a guanine nucleotide exchange factor for Ras that binds to grb2", Science **260**:1338-1343
	AI	Chen et al., 1993, "A murine CDC25/Ras-GRF-related protein implicated in Ras regulation", Devel. Genet. **14**:339-346
	AJ	Clauser et al., 1995, "Rapid mass spectrometric peptide sequencing and mass matching for characterization of human melanoma proteins isolated by two-dimensional PAGE", Proc. Natl. Acad. Sci. USA **92**:5072-5076
	AK	Cottrell, 1994, "Protein identification by peptide mass fingerprinting", Pept. Res. **7**:115-124
	AL	Dankort et al., 1997, "Distinct tyrosine autophosphorylation sites negatively and positively modulate neu-mediated transformation", Mol. Cell. Biol. **17**:5410-5425
	AM	Ebinu et al., 1998, "RasGRP, a Ras guanyl nucleotide- releasing protein with calcium- and diacylglycerol-binding motifs", Science **280**:1082-1086

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	AN	Ellis et al., 1995, "Phosphorylation-dependent complexes of p120 -specific GTPase-activating protein with p62 and p190", Methods In Enzymology **255**:179-192
	AO	Eng et al., 1994, "An approach to correlate tandem mass spectral data of peptides with amino acid sequences in a protein database", J. Am. Soc. Mass Spectrom. **5**:976-989
	AP	Fam et al., 1997, "Cloning and Characterization of Ras-GRF2, a novel exchange factor for Ras", Mol. Cell. Biol. **17**:1396-1406
	AQ	Fam et al., 1997, "The Ras-GRF2 gene maps to human chromosome 5 and murine chromosome 13 near the Ras-GAP gene", Genomics 39:118-120
	AR	Fan et al., 1998, "The exchange factor Ras-GRF2 activates Ras-dependent and Rac-dependent mitogen-activated protein kinase pathways", Curr. Biol. **8**:935-938
	AS	Farnsworth et al., 1995, "Calcium activation of Ras mediated by neuronal exchange factor Ras-GRF", Nature **376**:524-527
	AT	Fenn et al., 1990, "Electrospray ionization: principles and practice", Mass Spectrometry Reviews **9**:37
	AU	Gariboldi et al., 1994, "Genetic mapping of the mouse CDC25Mm gene, a Ras-specific guanine nucleotide-releasing factor, to chromosome 9", Genomics **21**:451-453
	AV	Gilbreth et al., 1998, "Negative regulation of mitosis in fission yeast by the shk1 interacting protein skb1 and its human homolog, Skb1Hs", Proc. Natl. Acad. Sci. USA **95**:14781-14786
	AW	Graham et al., 1977, "Characteristics of a human cell line transformed by DNA from human adenovirus type 5", J. Gen. Virol. **36**:59-74
	AX	Hall, 1994, "Small GTP-binding proteins and the regulation of the actin cytoskeleton", Annu. Rev. Cell Biol. **10**:31-54
	AY	Harlow and Lane, 1988, Antibodies: A Laboratory Manual (Cold Spring Harbor, Cold Spring Harbor)
	AZ	Hillenkamp et al., 1991, "Matrix-assisted laser desorption/ionization mass spectrometry of biopolymers", Anal. Chem. **63**:1193A-1203A
	BA	Krapivinsky et al., 1994, "Molecular characterization of a swelling-induced chloride conductance regulatory protein, pICln", Cell **76**:439-448
	BB	Krapivinsky et al., 1998, "pICln binds to a mammalian homolog of a yeast protein involved in regulation of cell morphology", J. Biol. Chem. **273**:10811-10814
	BC	Lowy and Willumsen, 1993, "Function and regulation of Ras", Ann. Rev. Biochem. **62**:851-891
	BD	Mann and Wilm, 1994, "Error-tolerant identification of peptides in sequence databases by peptide sequence tags", Anal. Chem. **66**:4390-4399

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	BE	McCormick, 1994, "Activators and effectors of Ras p21 proteins", Curr. Opin. Genet. Dev.
	BF	Millward et al., 1999, "Ndr protein kinase is regulated by phosphorylation on two conserved sequence motifs", J. Biol. Chem. **274**:33847-33850
	BG	Moran et al., 1991, "Protein-tyrosine kinases regulate the phosphorylation, protein interactions, and subcellular distribution of $p21^{Ras}$ GTPase activating protein", Mol. Cell. Biol. **11**:1804-1812
	BH	Nelson et al., 1994, "Mass determination of human immunoglobulin IgM using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry", Rapid Commun. Mass Spectrom. **8**:627-631
	BI	Ohtsuka et al., 1999, "Nrap GEP: A novel neural GDP/GTP exchange protein for Rap1 small G protein that interacts with Synaptic Scaffolding Molecule (S-SCAM)", Biochem. Biophys. Res. Commun. **265**:38-44
	BJ	Olson et al., 1995, "An essential role for Rho, Rac, and Cdc42 GTPases in cell cycle progression through G1", Science **269**:1270-1272
	BK	Papayannopoulos, 1995, "The interpretation of collision-induced dissociation tandem mass spectra of peptides", Mass Spect. Rev. 14:49-73
	BL	Pappin, 1997, "Peptide mass fingerprinting using MALDI-TOF mass spectrometry", Methods Mol. Biol. **64**:165-173
	BM	Patterson and Aebersold, 1995, "Mass spectrometric approaches for the identification of gel-separated proteins", Electrophoresis **16**:1791-1814
	BN	Patterson et al., 1996, "Application of combined mass spectrometry and partial amino acid sequence to the identification of gel-separated proteins", Electrophoresis **17**:877-891
	BO	Pawson, 1995, "Protein modules and signaling networks", Nature **373**:573-580
	BP	Pham et al., 2000, "CNRasGEF, a PDZ- and cNMP binding domain-containing guanine nucleotide-exchange factor, activates Ras in response to cAMP and cGMP", Current Biology **10**:555-558
	BQ	Pollack et al., 1999, "The human homologue of the yeast proteins Skb1 and Hsl7p interacts with Jak kinases and contains protein methyltransfeRase activity", J. Biol. Chem. **274**:31531-31542
	BR	Pu et al., 1999, "pICln inhibits snRNP biogenesis by binding core spliceosomal proteins', Mol. Cell. Biol. **19**:4113-4120
	BS	Schweighoffer et al., 1993, "Identification of a human guanine nucleotide-releasing factor (H-GRF55) specific for Ras proteins', Oncogene **8**:1477-1485
	BT	Scott and Pawson, 2000, "Cell communication: the inside story", Sci. Am. **282**:72-79
	BU	Shevchenko et al., 1997, "Rapid 'de novo' peptide sequencing by a combination of nanoelectrospray, isotopic labeling and a quadrupole/time-of-flight mass spectrometer", Rapid. Commun. Mass Spectrom. **11**:1015-1024

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	BV	Staub et al., 1996, "WW domains of Nedd4 bind to the proline-rich PY motifs in the epithelial Na+ channel deleted in Liddle's syndrome', EMBO J. **15**:2371-2380
	BW	Stone et al., 1991, "Construction and expression of linker insertion and site-directed mutants of the v-fps protein-tyrosine kinase', Methods Enzymol. **200**:673-692
	BX	Tang and Tang, 1998, "The 30-kD domain of protein 4.1 mediates its binding to the carboxyl terminus of pICln, a protein involved in cellular volume regulation", Blood **92**:1442-1447
	BY	Treisman, 1996, "Regulation of transcription by MAP kinase cascades", Curr. Op. Cell. Biol. **8**:205-215
	BZ	Tung et al., 1997, "A 54 kDa protein related to Ras-GRF expressed in the exocrine pancreas. Cell Tiss. Res. 289:505-515
	CA	Verde et al., 1998, "Fission yeast orb6, a ser/thr protein kinase related to mammalian rho kinase and myotonic dystrophy kinase, is required for maintenance of cell polarity and coordinates cell morphogenesis with the cell cycle", Proc. Natl. Acad. Sci. USA **95**:7526-7531
	CB	Wilkins et al., 1996, "Rapid protein identification using N-terminal "sequence tag" and amino acid analysis", Biochem. Biophys. Res. Commun. **221**:609-613
	CC	Wilm et al., 1996, "Femtomole sequencing of proteins from polyacrylamide gels by nano- electrospray mass spectrometry", Nature **379**:466-469
	CD	Yates et al., "Peptide sequencing by tandem mass spectrometry" Cell Biology: A Laboratory Handbook, vol. 4. (Academic Press, San Diego) pp. 529-538
	CE	Yates et al., 1995, "Method to correlate tandem mass spectra of modified peptides to amino acid sequences in the protein database", Anal. Chem. **67**:1426-1436
	CF	de Hoog et al., 2000, "Calmodulin-independent coordination of Ras and extracellular signal-regulated kinase action by Ras-GRF2", Mol. Cell. Biol. 20:2727-2733
	CG	de Hoog et al., 2001, "Ras binding ubiquitination of the Ras exchange factor Ras-GRF2", Mol. Cell. Biol. 21:2107-2117
	CH	Fam et al., 1997, "Mapping of the Ras-GRF2 gene (GRF2) to mouse chromosome 13C3-D1 and human chromosome 5q13, near the Ras-GAP gene", Genomics 39:118-120
	CI	Yagi et al., 1994, "The UAS of the yeast GAPDH promoter consists of multiple general functional elements including RAP1 and GRF2 binding sites", J. Vet. Med. Sci. 56:235-244

EXAMINER		DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP § 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to the applicant.